

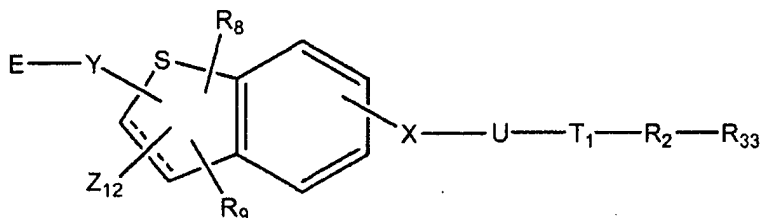
Amendments to the Claims

Please amend Claims 4, 50, 54, 55 and 115. Please cancel Claim 53. Please add new Claim 116. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

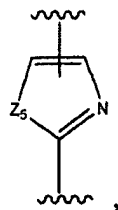
1-3. (Cancelled)

4. (Currently Amended) A compound represented by the following Structural Formula:



or a stereoisomer, pharmaceutically acceptable salt, or hydrate thereof, wherein:

(a) T1 is a moiety of formula



optionally substituted with

one substituent selected from C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R1'; or

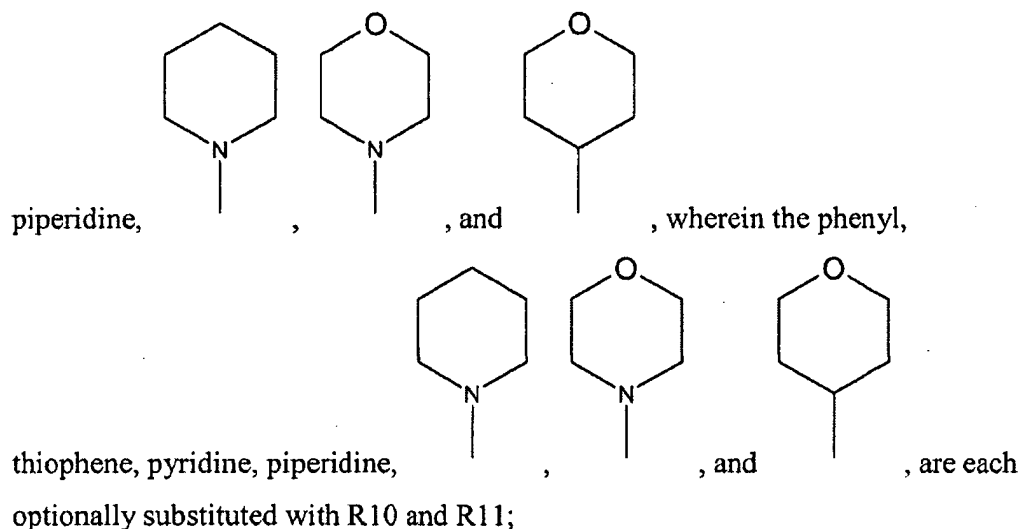
one substituent selected from ~~C₂-C₆ alkyl~~ C₃-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxy; and;

- (b) R1', R26, R27, R28, R31, Z14', and Z15' are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀₋₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉, NR₂₀SO₂R₂₁, SR₂₂, S(O)R₂₃, S(O)₂R₂₄, and S(O)₂N(R₂₅)₂; R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄ and R₂₅ are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (c) R₂ is selected from the group consisting of C₀-C₈ alkyl and C₁₋₆-heteroalkyl;
- (d) X is selected from the group consisting of a bond, O, S, S(O)₂ and N;
- (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker may be replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with R₃₀;
- (f) Y is selected from the group consisting of C, O, S, NH and a single bond;
- (g) E is C(R₃)(R₄)A or A and wherein
 - (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkynitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;
 - (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl-C₀₋₄ alkyl and C₁-C₆ alkyl, wherein such alkyl and arylalkyl are each optionally substituted with from one to two groups independently selected from R^{7'}; each R^{7'} is independently selected from halo, C₁-C₆ alkyl, and haloC₁-C₆ alkyl;
 - (iii) R₃ is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and
 - (iv) R₄ is selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀₋₄ alkyl, and R₃ and R₄ are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy,

cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R26;

- (h) Z5 is S or O;
- (i) Z12 is selected from the group consisting of hydrogen and -Z13C₀-C₃alkylZ14;
- (j) Z13 is selected from the group consisting of a single bond, CO, CO₂, CONZ15, and SO₂;
- (k) Z14 is selected from the group consisting of aryl and heteroaryl, wherein the aryl and heteroaryl is each optionally substituted with from one to three substituents independently selected from Z14';
- (l) Z15 is selected from the group consisting of hydrogen, aryl, and heteroaryl, wherein the aryl and heteroaryl is each optionally substituted with from one to three substituents independently selected from Z15';
- (m) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, oxo, sulfo, and halo;
- (n) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, oxo, sulfo, and OR29, and R8 and R9 together optionally combine to form a fused C5-C6 ring with the carbons to which they are attached, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C₁-C₄ alkyl;
- (o) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₀-C₆ alkyl-COOR12'', C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three independently selected from R28;

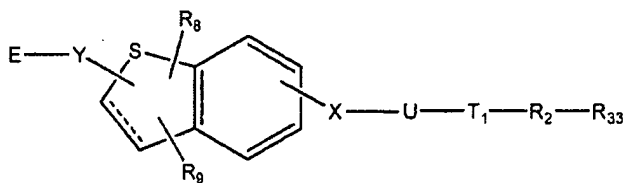
- (p) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (q) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (r) R33 is selected from the group consisting of phenyl, thiophene, pyridine,



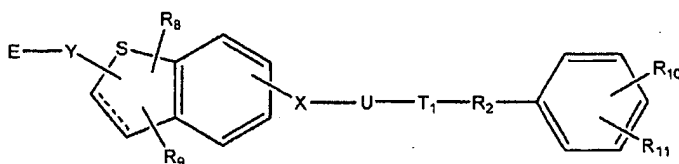
- (s) wherein "----" are each independently an optional bond to form a double bond at the indicated position.

5. (Cancelled)

6. (Previously Presented) The compound of Claim 4, wherein the compound is represented by the following Structural Formula:

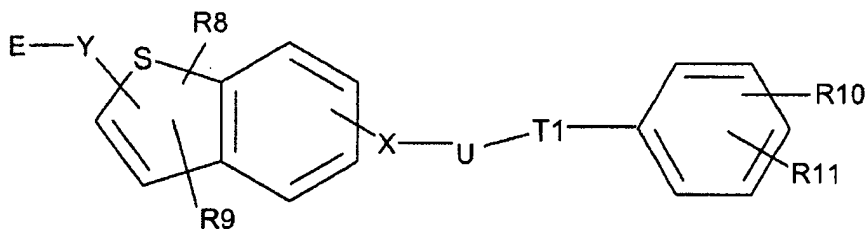


7. (Previously Presented) The compound of Claim 6, wherein the compound is represented by the following Structural Formula:



- 8-9. (Canceled)

10. (Previously Presented) The compound of Claim 7 wherein the compound is represented by the following Structural Formula:



11. (Previously presented) The compound of Claim 10 wherein:

X is -O-;

E is C(R3)(R4)CO₂H or CO₂H;

R1, R3, and R4 are each independently selected from the group consisting of hydrogen and C₁-C₂ alkyl;

R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR^{12''}, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, and C₁-C₆ haloalkyloxy; and
 U is saturated C₁-C₃ alkyl optionally substituted with C₁-C₃ alkyl.

12-45. (Cancelled)

46. (Previously Presented) A compound selected from the group consisting of:
- {6-[5-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-ylmethoxy]-benzo[b]thiophen-3-yl}-acetic acid;
 - {4-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-ylmethoxy]-benzo[b]thiophen-3-yl}-acetic acid;
 - {4-[5-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-ylmethoxy]-benzo[b]thiophen-3-yl}-acetic acid;
 - (6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (6-{1-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-yl]-ethoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-yl]-ethoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (R)-(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (S)-(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;
 - (R)-(4-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;

(*S*)-(4-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-propoxy}-benzo[b]thiophen-3-yl)-acetic acid;

(4-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-ethoxy}-benzo[b]thiophen-3-yl)-acetic acid;

Racemic-(4-{1-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-yl]-ethoxy}-benzo[b]thiophen-3-yl)-acetic acid;

(6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-4-yl]-propoxy}-benzofuran-3-yl)-acetic acid;

(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-yl]-propoxy}-benzofuran-3-yl)-acetic acid;

(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-yl]-propoxy}-benzofuran-3-yl)-acetic acid;

(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-yl]-ethoxy}-benzofuran-3-yl)-acetic acid;

{6-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-ylmethoxy]-benzofuran-3-yl}-acetic acid;

(6-{1-Methyl-1-[4-methyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-yl]-ethylsulfanyl}-benzofuran-3-yl)-acetic acid;

{6-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-ylmethylsulfanyl]-benzofuran-3-yl}-acetic acid;

(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-yl]-ethylsulfanyl}-benzofuran-3-yl)-acetic acid;

(6-{1-[4-Methyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-yl]-ethylsulfanyl}-benzofuran-3-yl)-acetic acid;

2-{6-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-ylmethoxy]-benzofuran-3-yl}-propionic acid;

2-(6-{2-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-oxazol-5-yl]-ethoxy}-benzofuran-3-yl)-propionic acid;

(6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-ethoxy}-benzofuran-3-yl)-acetic acid;

(*R*)-(6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-propoxy}-benzofuran-3-yl)-acetic acid (Isomer 2);
 (*S*)-(6-{2-[5-Methyl-2-(4-trifluoromethyl-phenyl)-thiazol-4-yl]-propoxy}-benzofuran-3-yl)-acetic acid;
 {5-[2-(5-Methyl-3-phenyl-pyrazol-1-yl)-ethoxy]-indol-1-yl}-acetic acid;
 (1-Methyl-6-{2-[3-methyl-1-(4-trifluoromethyl-phenyl)-1H-pyrazol-4-yl]-propoxy}-1H-indol-3-yl)-acetic acid;
 {5-[5-(4-Trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-indol-1-yl}-acetic acid;
 (5-{2-[3-Methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propoxy}-indol-1-yl)-acetic acid;
 {6-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-ylmethoxy]-benzo[*b*]thiophen-3-yl}-acetic acid; and
 2-(6-((4-tert-butyl-2-(4-(trifluoromethyl)phenyl)thiazol-5-yl)methylthio)benzo[*b*]thiophen-3-yl)acetic acid.

47-49. (Cancelled)

50. (Currently Amended) A method of treating a mammal in need of treatment for a disease, wherein the disease is treatable by activating a peroxisome proliferator activated receptor, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of the compound of Claim 4, wherein the disease is selected from diabetes mellitus, Syndrome X, and atherosclerosis.

51-53. (Cancelled)

54. (Currently Amended) The method of Claim [[53]] 50, wherein the disease is diabetes mellitus.

55. (Currently Amended) The method of Claim [[53]] 50, wherein the disease is Syndrome X.

56-100. (Cancelled)

101. (Previously Presented) A compound, wherein the compound is:

{6-[4-Isopropyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-ylmethoxy]-benzo[b]thiophen-3-yl}-acetic acid; or

2-(6-((4-tert-butyl-2-(4-(trifluoromethyl)phenyl)thiazol-5-yl)methylthio)benzo[b]thiophen-3-yl)acetic acid;

or a stereoisomer, pharmaceutically acceptable salt, or hydrate thereof.

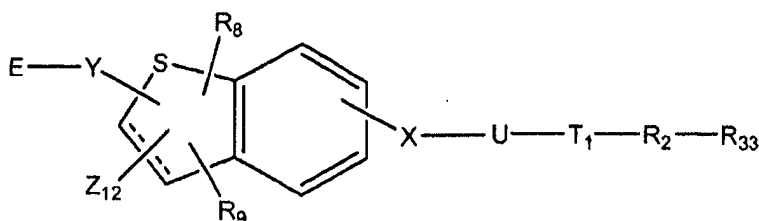
102-107. (Cancelled)

108. (Previously Presented) A method of treating a human subject in need of treatment for a disease selected from the group consisting of diabetes mellitus, Syndrome X, and atherosclerosis, comprising the step of administering to the subject in need thereof a therapeutically effective amount of the compound of Claim 101.

109-114. (Cancelled)

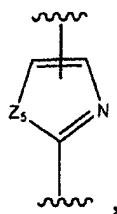
115. (Currently Amended) A method of treating a mammal in need of treatment for a disease, wherein the disease is treatable by activating a peroxisome proliferator activated receptor, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of the compound of Claim 46, disease selected from the group consisting of diabetes mellitus, Syndrome X, and atherosclerosis.

116. (New) A compound represented by the following Structural Formula:



or a stereoisomer, pharmaceutically acceptable salt, or hydrate thereof, wherein:

(s) T1 is a moiety of formula



optionally substituted with

one substituent selected from C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃₋₆ cycloalkylaryl-C₀₋₂-alkyl, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₆-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃₋₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R1'; or

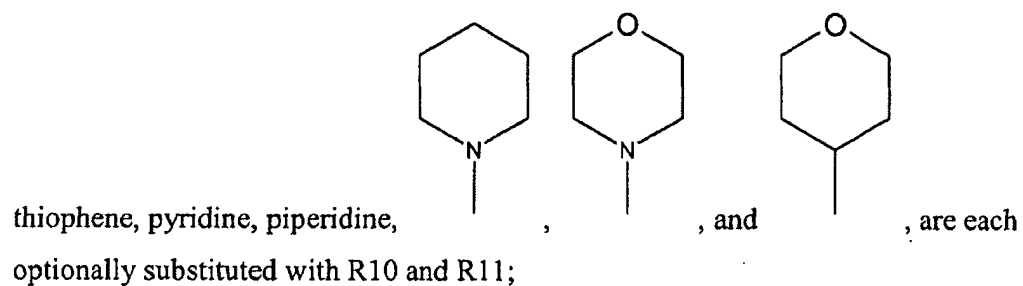
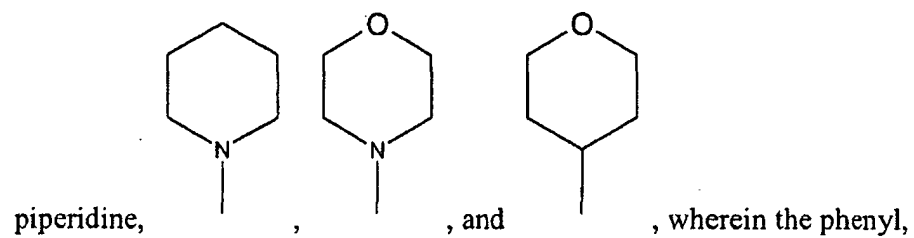
one substituent selected from C₁-C₆ haloalkyl, and C₁-C₆ alkyloxy; and;

- (t) R1', R26, R27, R28, R31, Z14', and Z15' are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃₋₇ cycloalkyl, aryloxy, aryl-C₀₋₄-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)₂R16, N(R17)₂, NR18C(O)R19, NR20SO₂R21, SR22, S(O)R23, S(O)₂R24, and S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (u) R2 is selected from the group consisting of C₀-C₈ alkyl and C₁₋₆-heteroalkyl;
- (v) X is selected from the group consisting of a bond, O, S, S(O)₂ and N;

- (w) U is an aliphatic linker wherein one carbon atom of the aliphatic linker may be replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with R30;
- (x) Y is selected from the group consisting of C, O, S, NH and a single bond;
- (y) E is C(R3)(R4)A or A and wherein
 - (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;
 - (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl-C₀-C₄ alkyl and C₁-C₆ alkyl, wherein such alkyl and arylalkyl are each optionally substituted with from one to two groups independently selected from R^{7'}; each R^{7'} is independently selected from halo, C₁-C₆ alkyl, and haloC₁-C₆ alkyl;
 - (iii) R3 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and
 - (iv) R4 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R26;
- (z) Z5 is S or O;
- (aa) Z12 is selected from the group consisting of hydrogen and -Z13C₀-C₃alkylZ14;
- (bb) Z13 is selected from the group consisting of a single bond, CO, CO₂, CONZ15, and SO₂;
- (cc) Z14 is selected from the group consisting of aryl and heteroaryl, wherein the aryl and heteroaryl is each optionally substituted with from one to three substituents independently selected from Z14';

- (dd) Z15 is selected from the group consisting of hydrogen, aryl, and heteroaryl, wherein the aryl and heteroaryl is each optionally substituted with from one to three substituents independently selected from Z15';
- (ee) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylene, oxo, sulfo, and halo;
- (ff) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylene, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, oxo, sulfo, and OR29, and R8 and R9 together optionally combine to form a fused C5-C6 ring with the carbons to which they are attached, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C₁-C₄ alkyl;
- (gg) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₀-C₆ alkyl-COOR12'', C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl-C₁-6-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-4-alkyl, aryl-C₁-6-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three independently selected from R28;
- (hh) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (ii) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl-C₁-6-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀-4-alkyl, aryl-C₁-6-heteroalkyl, heteroaryl-C₀-4-alkyl, and C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(jj) R33 is selected from the group consisting of phenyl, thiophene, pyridine,



wherein "----" are each independently an optional bond to form a double bond at the indicated position.